

Amendments to the Claims:

Please cancel claims 1-31 without disclaimer or prejudice to applicant's right to pursue the subject matter of these claims in a future continuation or divisional application.

Please add new claims 32-77 as set forth below.

32. (New) A method for treating a disease or disorder with an underlying dysregulation of emotional functionality comprising administering to a patient a compound having (i) a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and (ii) a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors, wherein the compound is administered to the patient in a dose ranging between 5 and 15 mg of the active ingredient.

33. (New) The method of claim 32, wherein the compound is PIPAMPERONE.

34. (New) The method of claim 33, wherein said disease or disorder is selected from the group consisting of anxiety disorders, eating disorders, premenstrual syndrome, somatoform disorders, factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep disorders, adjustment disorders, cognitive disorders, impulse control disorders, pervasive development, attention-deficit and disruptive behaviour disorders, substance-related disorders, personality disorders, psychological factors affecting medical conditions, malingering, antisocial behaviour, bereavement, occupational, identity, phase of life, academic problem, and problems related to abuse or neglect.

35. (New) The method of claim 32, comprising administering a second compound to the patient simultaneously with, separate from or sequential to administering a first compound as defined in claim 32, to augment the therapeutic effect of said second compound or to provide a faster onset of the therapeutic effect of said second compound.

36. (New) The method of claim 35, wherein said second compound has a therapeutic effect on a disease or disorder which is selected from the group consisting of mood disorders, anxiety disorders, schizophrenia and other psychotic disorders, eating disorders, premenstrual syndrome, somatoform disorders, factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep disorders, adjustment disorders, cognitive disorders, impulse control disorders, pervasive development, attention-deficit and disruptive behaviour disorders, substance-related disorders, personality disorders, psychological factors affecting medical conditions, malingering, antisocial behaviour, bereavement, occupational, identity, phase of life, academic problem, and problems related to abuse or neglect.

37. (New) The method of claim 35, wherein said first compound is administered daily at least one day before administering said second compound.

38. (New) The method of claim 35, wherein said second compound is a selective serotonin re-uptake inhibitor.

39. (New) The method of claim 38, wherein said selective serotonin re-uptake inhibitor is selected from the group consisting of CITALOPRAM, fluoxetine, venlafaxine,

fluvoxamine, paroxetine, sertraline, milnacipran and duloxetine, or a pro-drug or an active metabolite thereof, or a pharmaceutically acceptable salt thereof.

40. (New) The method of claim 39, wherein said serotonin re-uptake inhibitor is CITALOPRAM and is administered in a dose ranging between 10 and 40 mg of the active ingredient.

41. (New) A pharmaceutical composition comprising:

(a) a compound having (i) a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and (ii) a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors, and

(b) a selective serotonin re-uptake inhibitor,  
as a combined preparation for simultaneous, separate or sequential use for treating a disease or disorder with an underlying dysregulation of emotional functionality as defined in claim 36.

42. (New) A pharmaceutical composition according to claim 41 comprising:

(a) pipamperone in a dose ranging between 5 and 15 mg of the active ingredient,  
and

(b) citalopram in a dose ranging between 10 and 40 mg of the active ingredient.

43. (New) A method for treating a disease or disorder with an underlying dysregulation of emotional functionality comprising administering to a patient a first compound having (i) a selective affinity for the Dopamine-4 (D4) receptor with a pKi

value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and a second compound having (ii) a selective affinity for the 5-HT<sub>2A</sub> receptor with a pK<sub>i</sub> value equal to or higher than 8 towards the 5-HT<sub>2A</sub> receptor and less than 8 towards other 5HT receptors.

44. (New) The method of claim 43, wherein said disease or disorder is selected from the group consisting of mood disorders, anxiety disorders, schizophrenia and other psychotic disorders, eating disorders, premenstrual syndrome, somatoform disorders, factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep disorders, adjustment disorders, cognitive disorders, impulse control disorders, pervasive development, attention-deficit and disruptive behaviour disorders, substance-related disorders, personality disorders, psychological factors affecting medical conditions, malingering, antisocial behaviour, bereavement, occupational, identity, phase of life, academic problem, and problems related to abuse or neglect.

45. (New) The method of claim 43, wherein said first compound is selected from the group consisting of PIPAMPERONE, FANANSERIN, L-745,870, PNU-101387G and U-101387, and wherein said second compound is selected from the group comprising PIPAMPERONE, FANANSERIN, ORG 5222, ZOTEPINE, OLANZEPINE, CLOZAPINE, S16924, S18327, AMPEROZIDE, SERTINDOLE, MDL 100.907, TIOSPIRONE, FLUSPIRILENE, OCAPERIDONE, RISPERIDONE and ZIPRASIDONE, or a pro-drug or an active metabolite thereof, or a pharmaceutically acceptable salt thereof.

46. (New) The method of claim 43, wherein said compounds are administered to the patient in a dose ranging between 0.5  $\mu$ g and 300 mg for each of the active ingredients.

47. (New) The method of claim 43, comprising administering said compounds simultaneously with, separate from or sequential to administering a third compound to the patient to augment the therapeutic effect of said third compound or to provide a faster onset of a therapeutic effect of said third compound.

48. (New) The method of claim 47, wherein said third compound is a selective serotonin re-uptake inhibitor.

49. (New) The method of claim 48, wherein said selective serotonin re-uptake inhibitor is selected from the group consisting of CITALOPRAM, fluoxetine, venlafaxine, fluvoxamine, paroxetine, sertraline, milnacipran and duloxetine, or a pro-drug or an active metabolite thereof, or a pharmaceutically acceptable salt thereof.

50. (New) The method of claim 49, wherein said serotonin re-uptake inhibitor is CITALOPRAM and is administered in a dose ranging between 10 and 40 mg of the active ingredient.

51. (New) A pharmaceutical composition comprising:

(a) a compound having a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors,

(b) a compound having a selective affinity for the 5-HT<sub>2A</sub> receptor with a pKi value equal to or higher than 8 towards the 5-HT<sub>2A</sub> receptor and less than 8 towards other 5HT receptors, and

(c) a selective serotonin re-uptake inhibitor,

as a combined preparation for simultaneous, separate or sequential use for treating a disease or disorder with an underlying dysregulation of emotional functionality as defined in claim 44.

52. (New) A method for treating a disease or disorder with an underlying dysregulation of emotional functionality comprising administering to a patient a compound as defined in claim 32 where the compound is administered simultaneously with, separate from or sequential to administering a nor-epinephrine re-uptake inhibitor to said patient to augment the therapeutic effect of said nor-epinephrine re-uptake inhibitor or to provide a faster onset of the therapeutic effect of said nor-epinephrine re-uptake inhibitor.

53. (New) A method for treating a disease or disorder with an underlying dysregulation of emotional functionality comprising administering to a patient a first compound and a second compound as defined in claim 43 where said compounds are administered simultaneously with, separate from or sequential to administering a nor-epinephrine re-uptake inhibitor to said patient to augment the therapeutic effect of said nor-epinephrine re-uptake inhibitor or to provide a faster onset of the therapeutic effect of said nor-epinephrine re-uptake inhibitor.

54. (New) The method of claim 52, wherein the nor-epinephrine re-uptake inhibitor is selected from the group consisting of tandamine, pirandamine, ciclazindol, fluparoxan, lortalamine, talsupram, talopram, prindamine, nomifensine, viloxazine, tomoxetine, duloxetine, venlafaxine, milnacipran and reboxetine, or a pro-drug or an active metabolite thereof, or a pharmaceutically acceptable salt thereof.

55. (New) The method of claim 53, wherein the nor-epinephrine re-uptake inhibitor is selected from the group consisting of tandamine, pirandamine, ciclazindol, fluparoxan, lortalamine, talsupram, talopram, prindamine, nomifensine, viloxazine, tomoxetine, duloxetine, venlafaxine, milnacipran and reboxetine, or a pro-drug or an active metabolite thereof, or a pharmaceutically acceptable salt thereof.

56. (New) The method of claim 52, wherein the disease or disorder is selected from the group consisting of anxiety disorders, eating disorders, premenstrual syndrome, somatoform disorders, factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep disorders, adjustment disorders, cognitive disorders, impulse control disorders, pervasive development, attention-deficit and disruptive behaviour disorders, substance-related disorders, personality disorders, psychological factors affecting medical conditions, malingering, antisocial behaviour, bereavement, occupational, identity, phase of life, academic problem, and problems related to abuse or neglect.

57. (New) The method of claim 53, wherein the disease or disorder is selected from the group consisting of anxiety disorders, eating disorders, premenstrual syndrome, somatoform disorders, factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep disorders, adjustment disorders, cognitive disorders, impulse control disorders, pervasive development, attention-deficit and disruptive behaviour disorders, substance-related disorders, personality disorders, psychological factors affecting medical conditions, malingering, antisocial behaviour, bereavement, occupational, identity, phase of life, academic problem, and problems related to abuse or neglect.

58. (New) A pharmaceutical composition comprising:

(a) a compound having (i) a selective affinity for the Dopamine-4 (D4) receptor with a  $pK_i$  value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and (ii) a selective affinity for the 5-HT<sub>2A</sub> receptor with a  $pK_i$  value equal to or higher than 8 towards the 5-HT<sub>2A</sub> receptor and less than 8 towards other 5HT receptors and

(b) a nor-epinephrine re-uptake inhibitor,  
as a combined preparation for simultaneous, separate or sequential use for treating a disease or disorder with an underlying dysregulation of emotional functionality as defined in claim 44.

59. (New) A pharmaceutical composition comprising:

(a) a compound having a selective affinity for the Dopamine-4 (D4) receptor with a  $pK_i$  value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors,

(b) a compound having a selective affinity for the 5-HT<sub>2A</sub> receptor with a  $pK_i$  value equal to or higher than 8 towards the 5-HT<sub>2A</sub> receptor and less than 8 towards other 5HT receptors, and

(c) a nor-epinephrine re-uptake inhibitor,  
as a combined preparation for simultaneous, separate or sequential use for treating a disease or disorder with an underlying dysregulation of emotional functionality as defined in claim 44.

60. (New) A method for treating a disease or disorder with an underlying dysregulation of emotional functionality comprising administering to a patient a compound as defined in claim 32 where said compound is administered simultaneously



with, separate from or sequential to administering a neuroleptic agent to said patient to augment the therapeutic effect of said neuroleptic agent or to provide a faster onset of the therapeutic effect of said neuroleptic agent.

61. (New) A method for treating a disease or disorder with an underlying dysregulation of emotional functionality comprising administering to a patient a first compound and a second compound as defined in claim 43 where said compounds are administered simultaneously with, separate from or sequential to administering a neuroleptic agent to said patient to augment the therapeutic effect of said neuroleptic agent or to provide a faster onset of the therapeutic effect of said neuroleptic agent.

62. (New) The method of claim 60, wherein said neuroleptic agent is selected from the group consisting of chlorpromazine, haloperidol, perphenazine, thioridazine, mesoridazine, trifluoperazine, fluphenazine, clozapine, olanzapine, risperidone, ziprasidone, quetiapine, sertindole, aripiprazole, sonopiprazole, blonanserin, iloperidone, perospirone, raclopride, zotepine, DU-127090, ORG-5222, SM-13496, amisulpride, CP-361428, Lu 35-138, balaperidone, S-18327, WAY-135452, eplivanserin, E-5842, SR-31742, NE-100, osanetant, SR-141716, SR-48692, BSF-201640, BSF-190555, LAX-101a, sarizotan, CX-691 and SB-271046, or a pro-drug or active metabolite thereof, or a pharmaceutically acceptable salt thereof.

63. (New) The method of claim 61, wherein said neuroleptic agent is selected from the group consisting of chlorpromazine, haloperidol, perphenazine, thioridazine, mesoridazine, trifluoperazine, fluphenazine, clozapine, olanzapine, risperidone, ziprasidone, quetiapine, sertindole, aripiprazole, sonopiprazole, blonanserin, iloperidone, perospirone, raclopride, zotepine, DU-127090, ORG-5222, SM-13496, amisulpride, CP-

361428, Lu 35-138, balaperidone, S-18327, WAY-135452, eplivanserin, E-5842, SR-31742, NE-100, osanetant, SR-141716, SR-48692, BSF-201640, BSF-190555, LAX-101a, sarizotan, CX-691 and SB-271046, or a pro-drug or active metabolite thereof, or a pharmaceutically acceptable salt thereof.

64. (New) The method of claim 60, wherein said disease or disorder is selected from the group consisting of anxiety disorders, eating disorders, premenstrual syndrome, somatoform disorders, factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep disorders, adjustment disorders, cognitive disorders, impulse control disorders, pervasive development, attention-deficit and disruptive behaviour disorders, substance-related disorders, personality disorders, psychological factors affecting medical conditions, malingering, antisocial behaviour, bereavement, occupational, identity, phase of life, academic problem, and problems related to abuse or neglect.

65. (New) The method of claim 61, wherein said disease or disorder is selected from the group consisting of anxiety disorders, eating disorders, premenstrual syndrome, somatoform disorders, factitious disorders, dissociative disorders, sexual and gender identity disorders, sleep disorders, adjustment disorders, cognitive disorders, impulse control disorders, pervasive development, attention-deficit and disruptive behaviour disorders, substance-related disorders, personality disorders, psychological factors affecting medical conditions, malingering, antisocial behaviour, bereavement, occupational, identity, phase of life, academic problem, and problems related to abuse or neglect.

66. (New) A pharmaceutical composition comprising:

(a) a compound having (i) a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and (ii) a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors, and

(b) a neuroleptic agent,

as a combined preparation for simultaneous, separate or sequential use for treating a disease or disorder with an underlying dysregulation of emotional functionality as defined in claim 44.

67. (New) A pharmaceutical composition comprising:

(a) a compound having a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors,

(b) a compound having a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors, and

(c) a neuroleptic agent,

as a combined preparation for simultaneous, separate or sequential use for treating a disease or disorder with an underlying dysregulation of the emotional functionality as defined in claim 44.

68. (New) A method for treating a musculoskeletal disease or disorder comprising administering to a patient a compound as defined in claim 32 where said compound is administered simultaneously with, separate from or sequential to administering a COX-2

inhibitor to said patient to augment the therapeutic effect of said COX-2 inhibitor or to provide a faster onset of the therapeutic effect of said COX-2 inhibitor.

69. (New) A method for treating a musculoskeletal disease or disorder comprising administering to a patient a first compound and a second compound as defined in claim 43 where said compounds are administered simultaneously with, separate from or sequential to administering a COX-2 inhibitor to said patient to augment the therapeutic effect of said COX-2 inhibitor or to provide a faster onset of the therapeutic effect of said COX-2 inhibitor.

70. (New) The method of claim 68, wherein said COX-2 inhibitor is selected from the group consisting of celecoxib, rofecoxib, meloxicam, piroxicam, deracoxib, parecoxib, valdecoxib, etoricoxib, a chromene derivative, a chroman derivative, N-(2-cyclohexyloxynitrophenyl)methane sulfonamide, COX189, ABT963 and JTE-522, or a pro-drug or active metabolite thereof, or a pharmaceutically acceptable salt thereof.

71. (New) The method of claim 69, wherein said COX-2 inhibitor is selected from the group consisting of celecoxib, rofecoxib, meloxicam, piroxicam, deracoxib, parecoxib, valdecoxib, etoricoxib, a chromene derivative, a chroman derivative, N-(2-cyclohexyloxynitrophenyl)methane sulfonamide, COX189, ABT963 and JTE-522, or a pro-drug or active metabolite thereof, or a pharmaceutically acceptable salt thereof.

72. (New) The method of claim 68, wherein said disease or disorder is selected from the group consisting of rheumatoid arthritis, osteoarthritis and ankylosing spondylitis.

73. (New) The method of claim 69, wherein said disease or disorder is selected from the group consisting of rheumatoid arthritis, osteoarthritis and ankylosing spondylitis.

74. (New) A pharmaceutical composition comprising:

(a) a compound having (i) a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors, and (ii) a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors, and

(b) a COX-2 inhibitor,

as a combined preparation for simultaneous, separate or sequential use for treating a musculoskeletal disease or disorder.

75. (New) A pharmaceutical composition comprising:

(a) a compound having a selective affinity for the Dopamine-4 (D4) receptor with a pKi value equal to or higher than 8 towards the D4 receptor and less than 8 towards other Dopamine receptors,

(b) a compound having a selective affinity for the 5-HT2A receptor with a pKi value equal to or higher than 8 towards the 5-HT2A receptor and less than 8 towards other 5HT receptors, and

(c) a COX-2 inhibitor,

as a combined preparation for simultaneous, separate or sequential use for treating a musculoskeletal disease or disorder.

76. (New) A method for preparing a compound having a selective Dopamine-4 (D4) and 5-HT2A antagonist, reverse agonist or partial agonist activity comprising the following steps:

(a) measuring the selective affinity of a test compound to the D4 receptor and selecting a compound that has a pKi value equal to or greater than 8 towards the D4 receptor in respect to all the other Dopamine receptors, and measuring the selective efficacy of the selected compound to the D4 receptor and selecting a compound which is a selective antagonist, inverse agonist or partial agonist of the D4 receptor;

(b) measuring the selective affinity of a test compound to the 5-HT2A receptor and selecting a compound that has a pKi value equal to or greater than 8 towards the 5-HT2A receptor in respect to all the other 5HT receptors, and measuring the selective efficacy of the selected compound to the 5-HT2A receptor and selecting a compound which is a selective antagonist, inverse agonist or partial agonist of the 5-HT2A receptor;

(c) identifying a compound which is selected in (a) and (b); and

(d) preparing the compound identified in (c).

77. (New) A compound prepared by the method of claim 76.